

Section 1: Introduction

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1. Introduction

This section specifies the sources of procedural information available to study staff, the responsibilities of Investigators of Record (IoRs), and the process by which each site will be approved to initiate implementation of MTN-042B, *Assessing Baseline Pregnancy Outcomes in Sub-Saharan Africa*. Also included is information on required submissions to Institutional Review Boards and/or Ethics Committees (IRBs/ECs).

1.1 Current Protocol Specifications

The table below documents the history of the MTN-042B protocol, along with any Clarification Memos (CMs), Letters of Amendment (LoAs), and Full Amendments, if applicable, all of which are considered Essential Documents. A copy of each document should be available to staff and a copy should be maintained in site essential files. It is not necessary for sites to file copies of the below-mentioned documents in this manual.

Document	Date
MTN-042B Protocol, Version 1.0	16 JAN 2019

Sites are expected to operate under the protocol version and associated CMs and/or LoAs currently approved by relevant IRBs/ECs. To ensure this section reflects the current specifications of the protocol, upon issuance of any future protocol CM, LoA, or Protocol Amendment, specifications listed above will be updated accordingly. These documents are available on the MTN-042B webpage (<https://mtnstopshiv.org/research/studies/mtn-042b>). Further information on the content and required handling procedures for these documents is available in the Microbicide Trials Network (MTN) Manual of Operational Procedures (MOP), which is located on the MTN webpage <https://mtnstopshiv.org/resources/manual-operational-procedures>.

1.2 Sources of Procedural Information

The Study Specific Procedures (SSP) Manual serves to supplement the protocol. It does not replace or substitute the protocol or its contents. In the event this manual is inconsistent with the information and guidance provided in the protocol, the specifications in the protocol will take precedence. In the event study implementation questions are not adequately addressed by the study protocol or this manual or if any inconsistencies between the two documents are identified, please notify the MTN-042B Study Management Team at mtn042b-mgmt@mtnstopshiv.org.

Electronic versions of the SSP Manual, the MTN-042B protocol, and all other study implementation tools are available on the MTN-042B website:

<https://mtnstopshiv.org/research/studies/mtn-042b>

Note that all study documents can be searched electronically for key words and phrases using the “find” feature (CTRL+F). Sites are encouraged to become familiar with electronic searching to make specific guidance easier to locate in the study documents.

Please contact the MTN-042B management team for general questions on protocol implementation

Current contact details for all MTN-042B colleagues and collaborators, as well as study alias lists, can be found in the MTN directory at:

<https://mtnstopshiv.org/people/directory>

1.3 Investigator Responsibilities

MTN-042B must be conducted in accordance with the United States (US) Health and Human Service regulations (45 CFR 46); standards of the International Council on Harmonisation (ICH) Guideline for Good Clinical Practice (E6); Institutional Review Board/Independent Ethics Committee determinations; all applicable in-country, state, and local laws and regulations; and other applicable requirements (e.g., NIH, DAIDS) and institutional policies. Copies of all such regulations, policies, and guidelines should be maintained in on-site essential document files.

The Division of AIDS (DAIDS) policies ‘[Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials](#)’ and ‘[Requirements for Essential Documents at Clinical Research Sites Conducting DAIDS Funded and/or Sponsored Clinical Trials](#)’ are useful for interpreting and operationalizing the applicable regulations and guidelines in accordance with DAIDS expectations. These resources are also available on the MTN website under ‘Resources and Links’ (<http://www.mtnstopshiv.org/resources>).

The IoR at each study site must sign an Investigator Signature Form (Protocol Signature Page [PSP]) and a DAIDS IoR Form to formally indicate his/her agreement to conduct MTN-042B in accordance with the provisions of the study protocol, applicable US regulations, and MTN policies. The obligations and responsibilities assumed by the IoR when signing the DAIDS IoR Form are listed on the form itself, which is available on the DAIDS Regulatory Support Center (RSC) website. Note that no staff member should fulfill the IoR role in the IoR’s absence. Full responsibility and authority over the protocol by anyone other than the IoR may only take place if an additional DAIDS IoR Form is completed and submitted to DAIDS. A PSP must be signed by the IoR and uploaded to DPRS for all initial protocol versions, all full protocol amendments, and all LOAs.

An IoR may delegate his or her obligations and responsibilities for conducting MTN-042B procedures to other study staff members. However, in doing so, this delegation does not relieve the IoR of his/her ultimate responsibility for all study procedures performed and all study data collected. Delegation of IoR responsibilities must be formally documented throughout the period of study implementation on the site’s Delegation of Duties (DoD) log.

DoD logs must meet standards as outlined in the DAIDS [Delegation of Duties Log Policy](#) and use the DAIDS-provided DoD [Template](#) and [Instructions](#).

Consistent with the regulations, guidelines, and policies cited above, the site IoR must obtain and maintain IRB/EC approval of MTN-042B throughout the period of study implementation. Detailed information on IRB/EC submission, review, approval, and documentation requirements is located in the MTN MOP. All sites are encouraged to request an acknowledgement of receipt for all documents submitted to their IRBs/ECs and to request that IRBs/ECs note the effective and expiry dates of all approvals. Documentation of all correspondence to and from all responsible IRBs/ECs (i.e., complete copies of all submissions, responses, and approvals) must be maintained in on-site essential document files. Documentation of all IRB/EC approvals may also be requested by the MTN Leadership and Operation Center (LOC).

Note: Guidance outlined in the current DAIDS [Protocol Registration Manual](#) regarding which staff should be included on the DAIDS IoR form as sub-investigators should be followed. The manual outlines that staff who make a “direct and significant contribution to the data” should be included as sub-investigators. This includes “site personnel who have more than minimal involvement with the conduct of the research (performing study evaluations or procedures or providing intervention) or more than minimal study conduct-related contact with study patients or confidential study data, records, or specimens.” The CRS Leader should be included as a sub-investigator if this individual is not also the IoR at the site.

If there is a change in IoR after study activation, a revised DAIDS IoR Form and a new PSP should be submitted to the DAIDS Protocol Registration Office (PRO). Sites should follow guidance in the current DAIDS Protocol Registration Manual regarding procedures for a change in IoR with the DAIDS PRO. Incoming investigators should also complete IoR training and document the change in IoR on the study DoD log (per the instructions provided in the DAIDS DoD template instructions). In addition, they may need to complete an electronic financial disclosure form via the HANC system; investigators who need to complete a HANC financial disclosure will be contacted by MTN Regulatory with additional guidance. Outgoing investigators sign off all DoD log entries. Additionally, sites should notify FHI 360, MTN Regulatory, and their OCSO PO of the change and complete any other documentation requested.

1.4 Study Activation Process

Prior to undertaking any study procedures, each study site must complete the following:

- obtain approval to conduct MTN-042B from all required local regulatory authorities and IRBs/ECs,
- complete protocol registration procedures with the DAIDS RSC PRO, and
- complete study activation requirements, and be issued a Study Activation Notice from MTN LOC (FHI 360).

Information on these procedures can be found in the MTN MOP. Detailed information on the requirements of pre-implementation steps are summarized in the MTN-042B Activation Checklist. FHI 360 will notify sites (on a site-by-site basis), when all activation requirements have been met by issuing a Study Activation Notice.

1.5 IRB/EC Submissions

Figure 1-1 lists IRB/EC submission and approval requirements pertinent to MTN-042B. The study site is encouraged to request that their IRBs/ECs acknowledge receipt for all documents submitted to them, and to request that the IRBs/ECs note both the effective date and the expiry dates of all approvals. Procedures for IRB/EC communication must be documented in site-specific Standard Operating Procedures (SOPs). Documentation of all correspondence to and from all responsible IRBs/ECs (i.e., complete copies of all submissions, responses, and approvals) must be maintained in on-site essential document files. Documentation of all IRB/EC approvals may also be requested by the MTN LOC.

Figure 1-1: IRB/EC Submissions Required for MTN-042B

Documents to be submitted to IRB/EC	Written Approval Required*
Prior to study initiation:	
MTN-042B Protocol, Version 1.0	Yes
Investigator of Record current CV	No
Other documentation required/requested by the IRB/EC such as SOPs, CRFs, and questionnaires. For MTN-042B this may include the Data Abstraction Form.	If required by IRB/EC
During and following conduct of the study:	
Study status reports/updates (at least annually)	Yes
Protocol clarification memos (submission encouraged but not required by DAIDS)	No
Protocol amendments (including full amendments (to a new protocol version) and letters of amendment)	Yes
Protocol departures/deviations/violations (per IRB/EC requirements and/or as directed by DAIDS)	No
Investigator of Record current CV (if Investigator of Record changes during study)	No
Other documentation required/requested by the IRB/EC	If required by IRB/EC
Final study report/closure report	No

*Denotes approvals required by US regulations and GCP guidelines.